UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/075,987	02/13/2002	Maria Alexandra Glucksmann	MPI98-047CP2DV2M	9969

7590 10/05/2004

INTELLECTUAL PROPERTY GROUP
MILLENNIUM PHARMACEUTICALS INC
75 SIDNEY STREET
CAMBRIDGE, MA 02139

EXAMINER	
BRANNOCK, MICHAEL T	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 10/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/075,987	GLUCKSMANN ET AL.	
	Examiner	Art Unit	
	Michael Brannock	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *n/a*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 July 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *080202*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Status of Application: Claims and Amendments

Claims 24-44 are pending and under examination

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

Information Disclosure Statement

The information disclosure statement filed July 30, 2002 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because citations A9 and A12 lack sufficient description so as to lead the reader to the cited documents. The documents provided have been considered, however the citation will not be printed. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Sequence Disclosures

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reasons: the specification makes reference to specific polynucleotide and polypeptide sequences, see the Description of the Drawings, for example; these references must contain a sequence identifier of the form: SEQ ID NO: X. Appropriate correction is required.

Objections:

The disclosure is objected to because of the following informalities:

a) The specification is missing ATCC deposit numbers (page 4 for example).

b) The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, see page 20 for example. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons:

Claims 24-37 and 40-44 require detection of "modulation" of activity. It is unclear what limitations are placed on the claim by the presence of the word "modulation", i.e. are there properties that are to be detected other than inhibition or activation as in claims 38 and 39?

Claims 24, 25, 33-42 require the detection of "a 14273 polypeptide activity" without specifying exactly what this activity is supposed to be and the specification defines "a 14273 polypeptide activity" in only general terms and by way of examples which are insufficient to define what is and what is not to be considered "a 14273 polypeptide activity".

Claim Rejections - 35 USC § 101

Claims 24-44 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. Claims 24-44 are directed assays for identifying modulators of the activity of a polypeptide of called 14273. The specification asserts that the expression of the mRNA encoding the polypeptide is upregulated in cardiac myocytes during a mouse model of cardiac hypertrophy. Thus, it is reasonable to believe that the polynucleotides encoding the 14273 polypeptide would be useful in diagnostic assays to detect the amount of 14273 mRNA as it may correlate with cardiac hypertrophy. However the instant claims are directed to methods which simply invite the artisan to embark on a research plan to try to determine what activities the 14273 polypeptide might have and if there might be an activity that is relevant to cardiac hypertrophy. The instant specification puts forth that the polypeptide is useful in a screening method to determine what ligands may activate or inhibit the polypeptide and also to determine what the physiological effects of the polypeptide might be (see pages 5, 10, 30-34). This proposed use lacks a specific

and substantial utility. It is not a specific use because any integral membrane protein could be used in exactly the same way. Further, many polynucleotides are known in the art to encode polypeptides, yet the polypeptides have no known function or known ligands. Any of these orphan clones could be used in the manner described in the specification for the claimed polynucleotide.

Furthermore, the proposed use of the polypeptide to screen for ligands of the polypeptide or for biologic effects of the polypeptide is not a substantial utility. A substantial utility is a practical use which amounts to more than a starting point for further research and investigation and does not require or constitute carrying out further research to identify or reasonably confirm what the practical use might ultimately be. For example, an assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would be a practical use of the material. However, a method of trying to find a particular activity with no particular correlation with a disease would not constitute a substantial utility. Basic research, such as studying the properties of the claimed product or the mechanisms in which the product is involved, does not constitute a substantial utility.

The specification puts forth that the gene encoding the 14273 receptor maps to a region associated with dilated cardiomyopathy (10q21-23) A stated belief that a correlation may exist between the polypeptide and a particular disease is not sufficient guidance to use the claimed methods to establish that an activity of the polypeptide has anything to do with a particular disease; it merely defines a starting point for further research and investigation to search for an activity and then to search for an actual relationship, if any exists. One of ordinary skill in the art appreciates that many different diseases are also associated with 10q21-23. For example,

Bowles et al., *Human Genetics* 105(6)582-6, 1999, reported that human peptidyl-prolyl-cis-trans-isomerase mitochondrial precursor gene maps to this same region but is not a cause of dilated cardiomyopathy (see the Abstract). Therefore, the information provided in the specification amounts to no more than an invitation to one of skill in the art to perform research and investigation into any possible role the activity may have in disease. The search for a particular activity, or for the claimed methods to find compounds that modulate an activity, is simply an invitation to carry out further research and investigation so as to one day learn to what particular use these methods can be employed – if such can be found.

The instant application has failed to provide guidance as to what purpose one of skill in the art could use the claimed invention, other than as a starting point for further research and investigation.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24-44 are rejected under 35 U.S.C. § 112 first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Furthermore, should Applicant establish a substantial utility for the claimed methods, Applicant has not provided sufficient guidance as to how to make and use the methods commensurate with the scope that is claimed for the following reasons:

First, claim 27 requires that the activity be G-protein phosphorylation, the specification does not appear to contemplate such and neither would such be expected; rather it is probably Applicant's intention that the activity be 14273 polypeptide phosphorylation, i.e., it is commonly accepted that the GPCR and not the G-protein is phosphorlyated.

Second, the claims require that the methods be practiced under conditions suitable for modulation of the 14273 activity. As is it commonly understood, the activity of a GPCR is induced by binding to an external ligand, yet no ligand has been identified by the specification. It is well established that it may take years of intensive trial and error experimentation to find a ligand for a GPCR. Nor has the specification taught what G-protein(s) couple to the receptor, or what fragments provide any activity, and nor has the specification taught what particular activities could be detected. The specification has merely provided a generalized list of activities that certain GPCRs have been shown to have. No particular activities are asserted to be associated with the 14273 receptor activity. Thus the artisan is left to perform extensive trial and error research and investigation in the hope of finding a ligand, finding a G-protein, and finding a specific activity that can be measured.

"Tossing out the mere germ of an idea does not constitute enabling disclosure... [R]easonable detail must be provided in order to enable members of the public to understand and carry out the invention." Genentech, Inc. v. Novo Nordisk Inc., 108 F.3d 1361, 1366, 42 U.S.P.Q.2d 1001, 1005 (Fed. Cir. 1997).

Therefore, due to the large quantity of experimentation necessary to try to find a ligand for the polypeptide, to try to find a G-protein, and to try to find an activity in which to measure,

the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the state of the art which recognizes the difficulty in pairing a ligand with an orphan GPCR, and the breadth of the claims which encompass and an indeterminately large scope of possible activities for the polypeptide of which the claims require knowledge of, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 24-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims require that the methods be practiced under conditions suitable for modulation of the 14273 activity. As is it commonly understood, the activity of a GPCR is induced by binding to an external ligand, yet no ligand has been identified by the specification. It is well established that it may take years of intensive trial and error experimentation to find a ligand for a GPCR. Nor has the specification taught what G-protein(s) couple to the receptor, or what fragments provide any activity, and nor has the specification taught what particular activities could be detected. The specification has merely provided a generalized list of activities that certain GPCRs have been shown to have. No particular activities are asserted to be associated with the 14273 receptor activity. Thus one skilled in the art would not recognize that applicant was in possession of these fundamentals, enumerated above, required to practice the claimed invention.

Conclusion

No Claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, Ph.D., can be reached at (571) 272-0961.

Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

MB

ELIZABETH KEMMERER
PRIMARY EXAMINER

September 29, 2004